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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/782,721	02/12/2001	H. Michael Shepard	NB 2004.02; 060925-0402	5394

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EXAMINER	
CRANE, LAWRENCE E	
ART UNIT	PAPER NUMBER
1623	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/10/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/782,721	SHEPARD ET AL.	
	Examiner	Art Unit	
	L. E. Crane	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *August 28, 2006(amdt)*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *56,57,59-66,69,70,73-79,88 and 90* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *56,57,59-66,69,70,73-79,88 and 90* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 May 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/18/06; 5/15/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Claims **67, 86, 87 and 89** have been cancelled, claims **56-57, 62-63, 76-77 and 88** have been amended, the disclosure has not been further amended, and new claim **90** has been added as per the amendment filed August 28, 2006. Two additional Information Disclosure Statements (2 IDSs) filed April 18, 2006 and May 15, 2006 have been received with all cited references as of the date of this Office action.

Claims **56, 57, 59-66, 69-70, 73-79, 88 and 90** remain in the case.

Applicant is respectfully requested to disclose the application serial numbers, and patent numbers when applicable, of all related cases filed by instant applicants wherein related subject matter has been claimed.

Note to applicant: When a rejection refers to a claim **X** at line y, the line number "y" is determined from the claim as previously submitted by applicant in the most recent response including ~~lines deleted by line through~~.

Claim **62** is objected to because of the following informalities:

In claim **62** at line 45, the term "diasteriomeric" is a misspelling of -- diastereomeric --.

Appropriate correction is required.

Applicant's arguments filed August 28, 2006 have been fully considered but they are not persuasive.

Examiner notes with appreciation the correction of claim **63**. However, the above noted spelling error has not yet been corrected.

Claims **56 and 57** are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims **56 and 57** are directed to methods of "inhibiting" and "treating," respectively, wherein the particular disease to be inhibited or treated has not been specified. The functional

terms "hyperproliferative neoplastic cell(s)" are illustrative of the problem of excessive scope. These terms are the equivalent of laundry list disclosures which fail to meet the written description requirement because each, taken individually or taken together, "... would not 'reasonably lead' those skilled in the art to any particular species." (MPEP §2163 (A) at p. 2100-160, column 2, making reference to *In re Rushig*, 379 F2d 990, 995 (CCPA 1967).

Applicant's arguments filed August 28, 2006 have been fully considered but they are not persuasive.

The above grounds of rejection have not been narrowed further to reflect applicant's unwillingness to make significant amendments to narrow the instant claims, specifically by the replacement of functional terminology with structural formulae and by the elimination of subject matter that is entirely prospective. It is well known and established that "... law requires that disclosure in an application shall inform those skilled in the art how to use appellant's alleged discovery, not how to find out how to use it for themselves." *In re Gardner et al.*, 166 USPQ 138 (CCPA 1970).

The following paragraph is repeated from Examiner's response to applicant's arguments following the above rejection in the previous Office action.

Applicant argues that the scope is not excessive because the limitation "neoplastic cell that overexpresses thymidylate synthase" limits the scope to only diseases wherein the neoplasm meets the noted limitation. Examiner agrees that the limitation narrows the scope, but because it is functional, said limitation does not particularly point out the specific diseases to be treated and by its nature is prospective because all diseases which meet the limitation, whether known or unknown, are encompassed. Plainly applicant cannot enable the treatment of an unknown disease condition. Therefore, examiner respectfully requests narrowing of the instant claims scopes to encompass disease conditions which are enabled herein or by declaration evidence only.

Claims **56-57, 59-61 and 88** are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one of ordinary skill in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The fundamental issue here is whether practicing the full scope of the instant invention is possible without undue experimentation. As provided for in In re Wands (858 F.2d 731, 737; 8 USPQ 2d 1400, 1404 (Fed Cir. 1988) the minimum factors to be considered in determination of whether a conclusion of "undue experimentation" is appropriate are as follows:

A. The breadth of the claims as defined by the terms "hyperproliferative neoplastic cell(s)" is excessively broad because said term reads on multiple different disease conditions including all varieties of neoplasms (cancers cells). Only in claim **89** is the term limited to specific neoplastic diseases.

B. The nature of the invention as described in the specific examples is limited to a showing that a single compound, a phosphoramidated derivative of 5-bromovinylated 2'-deoxyuridine nucleoside is much more effective that the non-phosphoramidated BVDU base compound in treating certain specific neoplastic diseases, human breast carcinoma and human colon carcinoma in particular.

C. The state of the prior art; the extensive prior art of record, as presently understood and reviewed, does not anticipate or render obvious the treatment of carcinomas with a phosphoramidated BVDU.

D. The level of one of ordinary skill is defined by the need to understand organic synthesis, and the testing of compounds in *in vitro* cell culture.

E. The level of predictability in the art is low because only two closely related neoplastic disease conditions have been shown to be effectively inhibited by a phosphoramidated BVDU compound.

F. The amount of direction provided by the inventor is limited to showing how to make and administer a single phosphoramidated BVDU compound to cause inhibition of two closely related neoplastic disease conditions.

G. The existence of working examples is limited to a single compound administered to cells in in vitro culture infected by two closely related carcinomas.

H. The quantity of experimentation needed to make or use the invention based on the content of the disclosure would be excessive because the disclosure does not described how to effectively treat anything other than carcinoma in humans breast and colon tissue.

Applicant's arguments filed August 28, 2006 have been fully considered but they are not persuasive.

Applicant is referred to the response following the rejection above.

Claims **56, 57 and 62** are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims **56 and 57** at line 2, the term "neoplastic cells" is incomplete. Examiner suggests that the term should be amended to read -- one or more neoplastic cells in need thereof --. Applicant is also requested to note that the term "human cell" was defined by the Board of Patent Appeals and Interferences (BPAI) in *Ex parte Balzarini*, 21 USPQ 2d, 1892, 1898 (1991) (see p. 1898, column 2, "Rejection IV") and was found to have a scope encompassing any human cell from individual cells in culture to a living "human host."

Applicant's arguments with respect to claims **56 and 57** have been considered but are deemed to be moot in view of the new grounds of rejection.

In claim **62** at lines 43-44, the term "a phosphoryl derivative or a phosphoramidatyl derivative of a naturally-occurring amino acid" is indefinite because it fails to define with particularity the substituent groups within the metes and bounds of the instant claimed subject matter. Examiner suggests that a chemical structure or structures is/are essential for the ordinary practitioner to know what the subject matter being claimed herein really is.

Applicant's arguments with respect to claim **62** have been considered but are deemed to be moot in view of the new grounds of rejection.

The non-statutory double patenting rejection, whether of the obviousness-type or non-obviousness-type, is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent. *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA

1969); *In re Vogel,* 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Van Ornam,* 686 F. 2d 937, 214 USPQ 761 (CCPA 1982); *In re Longi,* 759 F.2d 887, 225 USPQ 645 (Fed. Cir 1985); and *In re Goodman,* 29 USPQ 2d 2010 (Fed. Cir. 1993).

A timely filed terminal disclaimer in compliance with 37 C.F.R. § 1.321(b) and (c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 C.F.R. §1.78(d).

Effective January 1, 1994, a registered attorney or agent or record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 C.F.R. §3.73(b).

Claims **56, 57, 59-66, 69-70, 73-79, 88 and 90** are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim ***1-12*** of U. S. Patent No. **6,495,553**. Although the conflicting claims are not identical, they are not patentably distinct from each other because the method of treatment and the alleged active ingredients are directed to substantially overlapping subject matter.

Claims **56, 57, 59-66, 69-70, 73-79, 88 and 90** are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims ***36-39*** of U. S. Patent No. **6,339,151**. Although the conflicting claims are not identical, they are not patentably distinct from each other because the method of treatment and the alleged active ingredients are directed to substantially overlapping subject matter.

Claims **56, 57, 59-66, 69-70, 73-79, 88 and 90** are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims ***1-7*** of U. S. Patent No. **6,245,750**. Although the conflicting claims are not identical, they are not patentably distinct from each other because the method of treatment and the alleged active ingredients are directed to substantially overlapping subject matter.

Claims **56, 57, 59-66, 69-70, 73-79, 88 and 90** are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims ***7-30 and 37-40*** of co-pending Application No. **10/119,927**. Although the conflicting claims are not

identical, they are not patentably distinct from each other because the compounds and the methods of treatment are overlapping with the instant claimed subject matter.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims **56, 57, 59-66, 69-70, 73-79, 88 and 90** are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims ***1 and 53-83*** of co-pending Application No. **10/681,418**. Although the conflicting claims are not identical, they are not patentably distinct from each other because the method of treatment and the alleged active ingredients are directed to substantially overlapping subject matter.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims **56, 57, 59-66, 69-70, 73-79, 88 and 90** are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims ***1-10*** of U. S. Patent No. **6,683,061** (PTO-892 ref. **AB**). Although the conflicting claims are not identical, they are not patentably distinct from each other because the compounds and the methods of treatment are overlapping with the instant claimed subject matter.

Claims **56, 57, 59-66, 69-70, 73-79, 88 and 90** are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims ***1-19*** of co-pending US Application No. **10/048,033**. Although the conflicting claims are not identical, they are not patentably distinct from each other because the compounds and the methods of treatment are overlapping with the instant claimed subject matter.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims **56, 57, 59-66, 69-70, 73-79, 88 and 90** are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims ***15-18, 21-23 and 27-50*** of co-pending Application No. **09/789,226**. Although the conflicting claims are not identical, they are not patentably distinct from each other because the compounds and the methods of treatment are overlapping with the instant claimed subject matter.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims **56, 57, 59-66, 69-70, 73-79, 88 and 90** are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims ***1-53*** of co-pending Application No. **11/034,036**. Although the conflicting claims are not identical, they are not patentably distinct from each other because the compounds and the methods of treatment are overlapping with the instant claimed subject matter.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims **56, 57, 59-61 and 88** are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims ***1 and 2*** of U. S. Patent No. **7,138,388** (See PTO-892 for citation). Although the conflicting claims are not identical, they are not patentably distinct from each other because the compounds and the methods of treatment are overlapping with the instant claimed subject matter.

Claims **56, 57, 59-66, 69-70, 73-79, 88 and 90** are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims ***1 -20*** of co-pending Application No. **11/516,457**. Although the conflicting claims are not identical, they are not patentably distinct from each other because the method of treatment and the alleged active ingredients are directed to substantially overlapping subject matter.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

One or more of claims **7-30 and 37-40** of this application conflict with claims ***7-30 and 37-40*** of Application No. **10/119,927**, claims ***1 and 53-83*** of co-pending Application No. **10/681,418**, claims ***1-36*** of copending Application No. **11/034,036**, and claims ***1-20*** of copending Application No. **11/516,457**, claims ***1-19*** of co-pending US Application No. **10/048,033**, and claims ***15-18, 21-23 and 27-50*** or copending Application No. **09/789,226**. 37 C.F.R. §1.78(b) provides that when two or more applications filed by the same applicant contain conflicting claims, elimination of such claims from all but one application may be required in the absence of good and sufficient reason for their retention during pendency in

more than one application. Applicant is required to either cancel the conflicting claims from all but one application or maintain a clear line of demarcation between the applications. See MPEP §822.

Applicant's arguments filed August 7, 2006 have been fully considered but they are not persuasive.

Applicant has acknowledged but has deferred effective responses to some of the above obviousness-type double patenting grounds of rejection. No terminal disclaimers have yet been received citing the above applications and patent. Several new rejections have been added. Therefore, the instant grounds of rejection found in the previous Office action have been maintained.

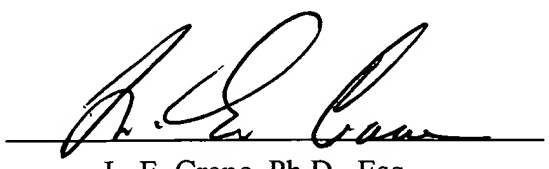
Papers related to this application may be submitted to Group 1600 via facsimile transmission(FAX). The transmission of such papers must conform with the notice published in the Official Gazette (1096 OG 30, November 15, 1989). The telephone number to FAX directly to Examiner's computer is 571-273-0651. The telephone number for submission of an official FAX to the USPTO is 571-273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner L. E. Crane whose telephone number is **571-272-0651**. The examiner can normally be reached between 9:30 AM and 5:00 PM, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ms. S. Anna Jiang, can be reached at **571-272-0627**.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is **571-272-1600**.

LECrane:lec
04/01/2007



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